

## REMARKS

In an Office Action dated April 20, 2010, the Examiner correctly stated the status of the claims; Claims 1 and 3-21 are pending, Claim 2 is cancelled, Claims 5, 6, 11, and 14-16 are withdrawn, and Claims 1, 3, 4, 7-10, 12, 13, and 17-21 are under consideration. The Examiner imposed new objections to the claims and maintained that the claims are obvious. As in the previous Action, Claim 21 is designated as "rejected" in the disposition of claims statement but is not included among any of the Examiner's rejections. Clarification of the status of Claim 21 is respectfully requested. A Request for Continued Examination accompanies this Response. In light of the amendments above and for the reasons noted below, Applicants respectfully request reconsideration.

### Objections

The Examiner objected to Claims 1, 3, 4, 7-10, 12, 17, and 19-21 for alleged failure to comply with certain formalities. Applicants amend the claims as indicated by the enclosed claim listing to address each of the Examiner's concerns and to improve clarity. Reconsideration is respectfully requested.

### Rejection under 35 U.S.C. §103(a)

The Examiner rejected Claims 1, 4, 7, 8, 10, 12, and 17-20 for alleged obviousness over Smith *et al.*, in view of either Thomson *et al.*, Jaynes *et al.*, or Chalitta-Eid, as evidenced by Tenner *et al.* or Tajima *et al.* further in view of Prasad *et al.* and Takada *et al.* Claims 3, 9, and 13 are rejected for alleged obviousness over Smith *et al.*, in view of either Jaynes *et al.* or Chalitta-Eid (as evidenced by Tenner *et al.*) and further in view of West *et al.*

The Examiner alleged that it would be obvious to electroporate clumps of hES cells because it was known to grow hES cells in clumps, as allegedly evidenced by Thomson, and known to electroporate adult rat parotid gland cells in clumps, as allegedly taught by Prasad. The Examiner relied on Tajima as allegedly teaching the use of a single pulse at 320 V and 250 µF.

The cited documents do not teach performing targeted modifications of human ES cells using electroporation under the recited conditions. The Examiner used impermissible hindsight in alleging that the cited documents directly led one of skill in the art to Applicants' invention.

Applicants understand that the documents are to be taken in combination. However, the Examiner relied on each document as teaching or suggesting individual recited claim limitations. Applicants emphasize that the individual documents do not teach or make obvious the recited claim limitations as characterized by the Examiner. As such, a combination of the cited documents cannot make obvious the invention as a whole.

Neither Thomson nor Prasad teach or suggest electroporating clumps of hES cells. Thomson teaches growing hES cells in colonies, not clumps. Thomson's Footnote 6 (not "reference 16," as the Examiner alleged, Office Action, page 6) explains that "inner cell mass-derived outgrowths were dissociated into clumps," which were subsequently replated onto murine fibroblasts to form colonies. Thus, the cells are cultured in colonies and only temporarily dissociated into clumps for transfer. The Examiner alleged that electroporation of hES in clumps was not an advancement in the art because Thomson teaches growing hES cells in clumps. Because Thomson does not teach growing hES cells in clumps, Thomson cannot make obvious electroporating hES cells in clumps.

Prasad does not teach that electroporation requires use of cell clumps, as the Examiner alleged (Office Action, page 6, third paragraph). In fact, Prasad teaches that rat parotid cells can be electroporated in clumps or in single-cell suspensions (Prasad, page 321, right column). Importantly, Prasad does not teach or suggest electroporating hES cells. Even if Prasad taught that electroporating clumps of cells was required for rat parotid cell electroporation, such teaching is irrelevant for hES cells because culture conditions for hES cells and rat parotid cells are entirely different. At the time of filing, a skilled artisan would not have had a reasonable expectation of success in using adult rat cell protocols to electroporate human embryonic stem cells, especially since murine ES cell protocols were known to not work for human ES cells.

Tajima does not teach a range "that touches or overlaps the claimed range," as the Examiner alleged (Office Action, page 7, last paragraph, emphasis added). In fact, Tajima does not teach any range, but rather a single microfarad value different from that recited in the claims. Claims 19-21 recite using a single 320 V and 200  $\mu$ F pulse, not 250  $\mu$ F. The Examiner failed to explain how using 250  $\mu$ F renders obvious using 200  $\mu$ F.

Applicants have made a diligent effort to place the pending claims into condition for

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Zwaka et al.

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Examiner: Maria Marvich

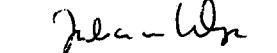
Date of Response: 20 August 2010

allowance. Should any issues remain, Applicants respectfully ask the Examiner contact the undersigned directly to resolve them expeditiously. For the reasons stated herein, this application is now believed to be in condition for allowance and such action is respectfully requested.

Fees

A Petition for an extension of time for one month accompanies this Response so the Response will be deemed to have been timely filed. Please charge the fee due to the Deposit Account 17-0055. Applicants include herewith a Request for Continued Examination and authorize the payment of the required fee. A separate form is attached confirming this request. No other fee is believed due in connection with this submission. If a fee is due, in this or any subsequent response, please charge the fee to the same Deposit Account.

Respectfully submitted,

  
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